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Original Article

Nasal carriage of *Staphylococcus aureus* among healthy adults

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Background and Purpose: Data on the carriage rate and antibiotic sensitivity pattern of *Staphylococcus aureus* strains prevalent in the community are not available for many developing countries including Malaysia. To estimate the extent of community *S. aureus* transmission, in particular methicillin-resistant *S. aureus* (MRSA), the prevalence of *S. aureus* nasal colonization in a population of healthy adults was determined. Factors associated with *S. aureus* nasal carriage and antibiotic sensitivity patterns of the isolates were also analyzed.

Methods: A cross-sectional study involving 346 adults was conducted. Nasal swabs were examined for the presence of *S. aureus*. Epidemiological information concerning risk factors for nasal carriage was also obtained. Antibiotic susceptibility testing was performed using the disk diffusion method according to the National Committee for Clinical Laboratory Standards guidelines. MRSA strains isolated were further subjected to pulse-field gel electrophoresis analysis.

Results: The prevalence of *S. aureus* nasal carriage was 23.4%. The findings also revealed that ex-smokers (95% confidence interval [CI] 1.08-6.32, p=0.033) and oral contraceptive users (95% CI 1.12-21.67, p=0.035) were more likely to harbor *S. aureus*. One person was colonized with MRSA, which was different from the hospital strain.

Conclusion: MRSA nasal colonization was found to be low outside of the health care environment. Smokers and oral contraceptive users have high nasal carrier rates.

Key words: Carrier state, methicillin, nasal mucosa, prevalence, resistance, *Staphylococcus aureus*

Introduction

Staphylococcus aureus is one of the most important human pathogens. It is a common cause of hospital and community-acquired infections worldwide. In humans, *S. aureus* colonization is mainly found in the anterior nares (40%) [1-3]. Nasal carriage of *S. aureus* is a potential source of infection and colonization often precedes infection. In general, nasal carrier rates among hospital personnel and patients (60-70%) are much higher as compared to those among community carriers (30-50%) [1].

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Treatment of staphylococcal infections has now become more challenging with the emergence of methicillin-resistant *S. aureus* (MRSA), which are often also multidrug resistant. MRSA has been reported with increasing frequency worldwide and is an important nosocomial pathogen. Because vancomycin is the main drug against MRSA, the emergence of *S. aureus* strains with intermediate resistance to vancomycin has raised concern about the possible spread of these strains [2]. Recently, MRSA has also been reported as a causative agent of community-acquired infections [3-5].

MRSA is an important nosocomial pathogen in Malaysia and several recent reports have shown that its prevalence as an endemic nosocomial pathogen is increasing. In a survey conducted in 14 hospitals in 1985-86, the prevalence rate was 10% to 25% [6]. The prevalence of MRSA isolates in several hospitals in

Malaysia in 1996 was even higher at 40% [7]. However, to date no community-acquired related infection has been documented. Furthermore, the most current data regarding *S. aureus* carriage and its antibiotic sensitivity pattern in Malaysia are based on studies carried out in hospital and outpatient settings, involving patients and hospital staff. In general, the prevalence of *S. aureus* nasal carriage from such settings in Malaysia varies from 45% to 76% [8]. Thus far, only one study has been published on the changing epidemiology and prevalence of antibiotic resistance among community-acquired *S. aureus* in Malaysia [8]. This study aimed to estimate the extent of *S. aureus* carriage, particularly MRSA, in a small community by performing nasal swabs, to determine its associated potential risk factors and the antibiotic susceptibility pattern of the isolates.

Methods

Patient selection and study design

We conducted a cross-sectional study involving students (both preclinical and health sciences students), staff, and visitors at the preclinical block of the Faculty of Medicine and Health Sciences, Universiti Putra, Malaysia. Healthy individuals over 18 years of age and willing to comply with the study protocol were deemed eligible for participation in the study. Individuals who were recently hospitalized were excluded. This study was approved by the Ethics Committee of the Faculty of Medicine and Health Sciences of the university.

Brochures describing the study were distributed from a booth within the faculty building. Informed consent was obtained from the participants. Epidemiological information was obtained by interviewing the participants at the time the nasal swabs were collected. These included demographic data (gender, race, and occupation) and data on clinical conditions (history of antibiotic usage in the past 2 weeks, history of chronic illnesses, smoking habits, and history of fever in the past 2 weeks). Data regarding occupation (students, staff, and visitors) and smoking habits (ex-smokers, current, and non-smokers) were also collected. Samples were collected from the anterior nares using sterile cotton wool swabs. It was estimated that a sample size of 339 participants was required at 5% level of significance, assuming that 30% of individuals in the community were nasal carriers. An estimated 5% was added to cover the participants whose carrier status could not be detected. A single proportion formula was used to determine the sample size. It was counter-checked by using Epi Info™ (Centers for Disease Control and Prevention, Atlanta, GA, USA) software version 6.04c.

Culture

Samples were cultured on mannitol salt agar (MSA). All colonies surrounded by yellow zones on MSA after 24-48 h of incubation at 37°C were selected. Colonies with pink or red zones were excluded. Identification of *S. aureus* was made on the basis of colony characteristics on MSA, Gram staining, and a positive tube coagulase test.

Antibiotic susceptibility testing

Disc diffusion method was performed according to National Committee for Clinical Laboratory Standards guidelines [9]. Single colonies were selected and cultured in Mueller-Hinton broth to prepare the inoculum. Mueller-Hinton agar was inoculated with a sterile swab dipped into the inoculum adjusted to the same density as 0.5 MacFarland turbidity standard. Inoculated plates were left to dry before the application of antibiotic discs. The plates were then inverted and incubated at 35°C for 16-18 h, and the plate containing oxacillin was incubated for 24 h. The isolates were tested against 14 antibiotics, namely penicillin (10 U), oxacillin (1 μg), gentamicin (10 μg), fusidic acid (10 μg), erythromycin (15 μg), ciprofloxacin (5 μg), tetracycline (30 μg), chloramphenicol (30 μg), clindamycin (2 μg), rifampicin (5 μg), cotrimoxazole (trimethoprim/sulfamethoxazole, 1.25/23.75 μg), amoxicillin/clavulanic acid (20/10 μg), vancomycin (30 μg), and mupirocin (5 μg). *S. aureus* American Type Culture Collection 25923 was used as control. The antibiotic discs were obtained from Oxoid (Oxoid Limited, Hampshire, UK).

Pulsed-field gel electrophoresis

Information on any MRSA strain isolated was submitted to the Department of Medical Microbiology, Faculty of Medicine, University of Malaya (a reference center) for pulsed-field gel electrophoresis.

Statistical analysis

Statistical Package for the Social Sciences (SSPS) for Windows (Version 12.0; SPSS, Chicago, IL, USA) software was used for the statistical analysis of epidemiological data. Frequency and percentage were presented for categorical data. Chi-squared, Fisher's exact, and simple logistic regression tests were applied to determine potential factors associated with *S. aureus*

nasal carriage. Multiple logistic regressions were used to identify the associated factors. Likelihood ratio test was used to determine the significance of the variable. Fit of the model was checked by Hosmer and Lemeshow test and overall classification percentage. The findings were presented with crude and adjusted odds ratio, 95% confidence interval (CI), Wald statistics, and corresponding *p* value. The level of significance was set at 0.05 using the two-tailed method.

Results

Out of 926 individuals approached, 346 agreed to participate. These comprised 120 males (34.7%) and 226 females (65.3%) with ages ranging from 19 to 68 years (mean age, 25.3 ± 8.7 years). None of the participants were ever hospitalized and most stayed on campus. Overall nasal carriage of *S. aureus* in this study population was 23.4% (81/346).

Table 1 shows univariate analysis of potential risk factors for *S. aureus* carriage. In the univariate analysis, staff was found to have a lower risk of *S. aureus* nasal carriage as compared to the other occupation groups. There was no difference between carriers and non-carriers with regard to fever or antibiotic usage in the past 2 weeks, skin disease, diabetes mellitus, rhinitis, and use of oral contraceptives or hormonal therapy. There was no association between *S. aureus* carrier state and smoking habits.

Using simple logistic regression analysis, staff were found to have a lower risk of carriage as compared to visitors. However, it was not found to be significant by multivariate analysis. For students, it was not significant by both simple and multiple logistic regression analysis. By multivariate analysis (Table 2), independent factors such as oral contraceptive use and ex-smoker were associated with *S. aureus* carriage. Those who used oral contraceptives were nearly 5 times more likely to be colonized with *S. aureus* as compared to non-users (odds ratio [OR] = 4.92, 95% CI 1.12-21.67, p=0.035). Ex-smokers (OR = 2.61, 95% CI 1.08-6.32, p=0.033) were found to be 2.5 times more likely to harbor *S. aureus* as compared to non-smokers.

Each sample positive for *S. aureus* was considered as one strain. A total of 81 strains were isolated. The antibiotic sensitivity pattern of these strains is shown in Table 3. As expected, a high penicillin resistance rate (82.7%) was observed among the strains. Low rates of resistance were expressed to clindamycin (2.5%), amoxicillin/clavulanic acid (2.5%), mupirocin (2.5%), chloramphenicol (1.2%), and rifampicin (1.2%). None of the strains were resistant to cotrimoxazole and vancomycin.

Table 1. Univariate analysis of potential factors for *Staphylococcus aureus* nasal carriage among healthy adults

Factor	*Staphylococcus aureus* Positive No. (%)	*Staphylococcus aureus* Negative No. (%)	*p*
Age (years)			
<30	70 (24.1)	220 (75.9)	0.726[a]
30-50	8 (18.6)	35 (81.4)	
>50	3 (23.1)	10 (76.9)	
Gender			0.611[a]
Male	30 (25.0)	90 (75.0)	
Female	51 (22.6)	175 (77.4)	
Race			
Malay	50 (23.4)	164 (76.6)	0.173[a]
Chinese	27 (27.6)	71 (72.4)	
Indian and others	4 (11.8)	30 (88.2)	
Occupation			
Student	64 (25.8)	184 (74.2)	0.037[a]
Staff	14 (15.2)	78 (84.8)	
Others	3 (50.0)	3 (50.0)	
Fever in past 2 weeks			
Absent	73 (24.7)	223 (75.3)	0.181[a]
Present	8 (16.0)	42 (84.0)	
Antibiotic in past 2 weeks			
Absent	79 (24.2)	247 (75.8)	0.181[b]
Present	2 (10.0)	18 (90.0)	
Skin disease			
Absent	78 (23.6)	252 (76.4)	0.772[b]
Present	3 (18.8)	13 (81.2)	
Rhinitis			
Absent	79 (23.9)	251 (76.1)	0.378[b]
Present	2 (12.5)	14 (87.5)	
Oral contraceptive			
Did not use	77 (22.8)	260 (77.2)	0.222[b]
Used	4 (44.4)	5 (55.6)	
Wound that does not heal			
Absent	78 (23.1)	260 (76.9)	0.396[b]
Present	3 (37.5)	5 (62.5)	
Smoking habit			
Non-smoker	69 (22.2)	242 (77.8)	0.125[b]
Ex-smoker	10 (40.0)	15 (60.0)	
Current smoker	2 (20.0)	8 (80.0)	

[a]Pearson chi-squared test applied.
[b]Fisher's exact test applied.

Resistance to 3 or more antibiotics was noted in 2 isolates (2.5%) — one of which was MRSA. This strain was also resistant to penicillin, gentamicin, fusidic acid, tetracycline, clindamycin, mupirocin, and rifampicin. The MRSA strain was isolated from a 23-year-old student, who had not visited any hospitals or taken antibiotics in the weeks prior to sampling. The strain

Table 2. Simple and multiple logistic regression analysis showing factors associated with *Stapylococcus aureus* infection

Factor	Simple logistic regression			Multiple logistic regression[a]		
	Crude OR	95% CI	*p*	Adjusted OR	95% CI	*p*
Smoking habit						
Non-smoker	1	-	-	1	-	-
Ex-smoker	2.34	(1.01, 5.44)	0.048	2.61	(1.08, 6.32)	0.033
Current smoker	0.88	(0.18, 4.23)	0.870	0.42	(0.37, 11.03)	0.418
Oral contraceptive						
Did not use	1	-	-	1	-	-
Used	2.70	(0.71, 10.31)	0.146	4.92	(1.12, 21.67)	0.035
Occupation						
Others	1	-	-	1	-	-
Students	0.35	(0.07, 1.77)	0.203	0.58	(0.10, 3.25)	0.531
Staff	0.18	(0.03, 0.98)	0.047	0.22	(0.04, 1.34)	0.100

Abbreviations: OR = odds ratio; CI = confidence interval

[a]Backward stepwise multiple logistic regression applied. Fit of the model was checked by Hosmer Lemeshow test (p=0.046) and overall correct classification percentage (77.2%).

was further confirmed as MRSA and demonstrated a different PFGE pattern when compared with MRSA strains isolated in the hospital.

Discussion

The nasal carriage of *S. aureus* varies depending on the different populations studied, the use of different culture techniques and different interpretation guidelines. In general, the hospital population harbors a higher carriage rate as compared to community carriers. In Malaysia, a study conducted at a rural hospital revealed an *S. aureus* carriage prevalence of 55% within the outpatient community and 76% within the hospital staff [10]. Another local study similar to ours reported an *S. aureus* carriage rate of 29% among healthy pre-clinical medical students [9]. However, the carriage rate in the present study cannot be generalized because the sample population was a select community, comprising mainly students at a small facility. Some medical students and a few lecturers practising in hospitals or clinics may have acquired the strain in the hospitals.

Table 3. Antibiotic sensitivity pattern of 81 strains of *Staphylococcus aureus* isolated from nasal carriers

Antibiotics	S No. (%)	I No. (%)	R No. (%)	N
Penicillin	14 (17.3)	-	67 (82.7)	81
Oxacillin	80 (98.8)	0 (0)	1 (1.2)	81
Gentamicin	79 (97.5)	0 (0)	2 (2.5)	81
Fusidic acid	77 (95.0)	2 (2.5)	2 (2.5)	81
Erythromycin	61 (75.3)	18 (22.2)	2 (2.5)	81
Ciprofloxacin	70 (86.4)	11 (13.6)	0 (0)	81
Tetracycline	53 (94.6)	0 (0)	3 (5.4)	56
Chloramphenicol	77 (95.1)	3 (3.7)	1 (1.2)	81
Clindamycin	78 (96.3)	1 1.2)	2 (2.5)	81
Rifampicin	80 (98.8)	0 (0)	1 (1.2)	81
Cotrimoxazole	81 (100)	0 (0)	0 (0)	81
Amoxicillin/ clavulanic acid	79 (97.5)	-	2 (2.5)	81
Vancomycin	81 (100)	-	0 (0)	81
Mupirocin	79 (97.5)	-	2 (2.5)	81

Abbreviations: S = susceptible; I = intermediate; R = resistant; N = total number tested

Our questionnaire was designed to establish any demographic and associated factors related to nasal carriage of *S. aureus*. Consistent with previous reports, we found that smoking, particularly among ex-smokers, was associated with *S. aureus* colonization. Smoking is known to alter the respiratory mucosal surface, facilitating the binding of potential pathogens, particularly *Streptococcus pneumoniae* and *Haemophilus influenzae*, and to a lesser extent *S. aureus*. This leads to an increased risk of airway colonization and development of pneumonia [11,12]. Raman et al also found that pneumococcal adherence in some ex-smokers remained high for up to 3 years after smoking cessation [13]. However, the etiological basis of this observation is unknown.

Our data also indicate that oral contraceptive users are at increased risk of harboring *S. aureus* nasal carriage. This finding was contrary to an earlier report of an antistaphylococcal effect on oral contraceptive steroids [14]. As there is a scarcity of data on this specific interaction, further studies are required to determine the actual relationship of oral contraceptives to *S. aureus* nasal carriage.

We found that the other variables studied were not risk factors for colonization of *S. aureus*. This was contrary to some findings of studies conducted 30-40 years ago. *S. aureus* carriage rates vary among different ethnic groups and are dependent on age [1,2,15-17]. Further, our study showed no variation in carrier rates among different races; however, the study population was predominantly Malay. In addition, studies have shown that certain chronic illnesses such as diabetes, rhinitis, and skin diseases result in a higher *S. aureus* carriage [1,2,18,19]. However, most of these studies were hospital-based or outpatient clinic-based rather than community-based. In support of this view, in one community-based study, Boyko et al found similar *S. aureus* carriage rates among patients with diabetes and healthy individuals, in contrast with an earlier clinic-based study [20].

In this study, the low prevalence of MRSA nasal carriage in a healthy population appears to contrast with the diverse dissemination of methicillin-sensitive *S. aureus* (MSSA). From 346 nasal swabs collected, only 1 MRSA isolate was identified while 80 persons were found to be nasal carriers for MSSA. The MRSA strain was isolated from a healthy individual who had no previous history of hospitalization and antibiotic intake prior to the sampling. However, history of contact with hospitalized persons was not available. The lack of community-acquired MRSA observed may reflect the difficulty of clonal spread in the absence of the strong selective advantage of drug resistance because, without selection, only a small portion of a given population will go on to establish itself in new environments [21]. Furthermore, MRSA strains are known to exhibit lower adherence to the nasal mucosa, rendering isolation of these strains from colonized nares seemingly more difficult [22].

A comparison of antibiotic sensitivity patterns of *S. aureus* in the community in Malaysia from previous studies with those obtained in the present study is shown in Table 4. Cloxacillin remains the antibiotic of choice in the treatment of beta-lactamase-producing *S. aureus* infection. Vancomycin is active against both MRSA and fusidic acid-resistant strains, and should be reserved for these cases. In general, *S. aureus* strains from community-based studies [10], including ours, were more susceptible to non-beta-lactam antibiotics as compared to those from studies based in health-care settings [9,23-25]. In our study, the MRSA isolated was also a mupirocin-resistant strain. This concurs with earlier findings that the rate of mupirocin resistance in MRSA is still low in Malaysia; in a surveillance project for monitoring antimicrobial resistance, 5 strains out of 400 MRSA isolated from 10 hospital laboratories in Malaysia were resistant to this topical antibiotic [26]. Hence, administration of mupirocin to eliminate nasal carriage of *S. aureus* should be carried out in select groups and for short courses only in order to prevent widespread resistance.

The high nasal carrier rates of *S. aureus* found among smokers and oral contraceptive users need

Table 4. Comparison of antibiotic resistant patterns of *Staphylococcus aureus* in Malaysia from published sources (1967-2003) with the present study (2004)

Types of community	HS	OP	OP	OP	HA	HA
Year of publication (reference)	1969 (23)	1971 (24)	1986 (25)	1995 (9)	2003 (10)	2004 (present study)
Penicillin	24.0	55.0	70.0	91.3	79.4	82.7
Methicillin	-	1.0	20.0	0.0	0.0	1.2
Gentamicin	-	-	0.0	-	0.0	2.5
Fusidic acid	-	-	10.0	6.5	11.8	2.5
Erythromycin	-	-	20.0	13.3	8.8	2.5
Ciprofloxacin	-	-	-	-	5.9	0
Tetracycline	23.0	44.0	15.0	23.4	5.9	5.4
Chloramphenicol	7.0	14.0	-	3.4	2.9	1.2
Clindamycin	-	-	-	1.8	-	2.5
Rifampicin	-	-	-	-	0	1.2
Cotrimoxazole	-	-	0	2.8	0	0
Amoxicillin/clavulanic acid	-	-	-	-	0	2.5
Vancomycin	-	-	0	-	0	0
Mupirocin	-	-	-	-	0	2.5

Abbreviations: HS = healthy schoolchildren; OP = outpatients; HA = healthy adults; - = not done

to be emphasized for public education. This study also showed that the spread of MRSA is still limited in this community of healthy adults. This could probably account for the lack of community-acquired MRSA-related infections documented in Malaysia. However, the results of this study cannot be generalized as it was a cross-sectional study involving a selected community in a particular area of Malaysia. In addition, there was no proper sampling method applied and therefore the findings, may only represent the community selected in this study. A more comprehensive study involving a larger population should be conducted to represent the Malaysian population.

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